

# SEQUENCE LISTING

<110> Amgen Inc.

<120> Crystal of a Kinase-Ligand Complex and Methods of Use

<130> A-747A

<140> US 09/574,559

<141> 2000-05-19

<150> US 09/574,630

<151> 2000-05-19

<150> US 60/134,965

<151> 1999-05-19

<160> 11

<170> PatentIn version 3.1

<210> 1

<211> 508

<212> PRT

<213> Homo sapiens

<400> 1

Gly Cys Gly Cys Ser Ser His Pro Glu Asp Asp Trp Met Glu Asn Ile  
1 5 10 15

Asp Val Cys Glu Asn Cys His Tyr Pro Ile Val Pro Leu Asp Gly Lys  
20 25 30

Gly Thr Leu Leu Ile Arg Asn Gly Ser Glu Val Arg Asp Pro Leu Val  
35 40 45

Thr Tyr Glu Gly Ser Asn Pro Pro Ala Ser Pro Leu Gln Asp Asn Leu  
 50 55 60

Val Ile Ala Leu His Ser Tyr Glu Pro Ser His Asp Gly Asp Leu Gly  
 65 70 75 80

Phe Glu Lys Gly Glu Gln Leu Arg Ile Leu Glu Gln Ser Gly Glu Trp  
 85 90 95

Trp Lys Ala Gln Ser Leu Thr Thr Gly Gln Glu Gly Phe Ile Pro Phe  
 100 105 110

Asn Phe Val Ala Lys Ala Asn Ser Leu Glu Pro Glu Pro Trp Phe Phe  
 115 120 125

Lys Asn Leu Ser Arg Lys Asp Ala Glu Arg Gln Leu Leu Ala Pro Gly  
 130 135 140

Asn Thr His Gly Ser Phe Leu Ile Arg Glu Ser Glu Ser Thr Ala Gly  
 145 150 155 160

Ser Phe Ser Leu Ser Val Arg Asp Phe Asp Gln Asn Gln Gly Glu Val  
 165 170 175

Val Lys His Tyr Lys Ile Arg Asn Leu Asp Asn Gly Gly Phe Tyr Ile  
 180 185 190

Ser Pro Arg Ile Thr Phe Pro Gly Leu His Glu Leu Val Arg His Tyr  
 195 200 205

Thr Asn Ala Ser Asp Gly Leu Cys Thr Arg Leu Ser Arg Pro Cys Gln  
 210 215 220

Thr Gln Lys Pro Gln Lys Pro Trp Trp Glu Asp Glu Trp Glu Val Pro  
 225 230 235 240

Arg Glu Thr Leu Lys Leu Val Glu Arg Leu Gly Ala Gly Gln Phe Gly  
 245 250 255

Glu Val Trp Met Gly Tyr Tyr Asn Gly His Thr Lys Val Ala Val Lys  
 260 265 270

Ser Leu Lys Gln Gly Ser Met Ser Pro Asp Ala Phe Leu Ala Glu Ala  
 275 280 285

Asn Leu Met Lys Gln Leu Gln His Gln Arg Leu Val Arg Leu Tyr Ala  
 290 295 300

Val Val Thr Gln Glu Pro Ile Tyr Ile Ile Thr Glu Tyr Met Glu Asn  
305 310 315 320

Gly Ser Leu Val Asp Phe Leu Lys Thr Pro Ser Gly Ile Lys Leu Thr  
325 330 335

Ile Asn Lys Leu Leu Asp Met Ala Ala Gln Ile Ala Glu Gly Met Ala  
340 345 350

Phe Ile Glu Glu Arg Asn Tyr Ile His Arg Asp Leu Arg Ala Ala Asn  
355 360 365

Ile Leu Val Ser Asp Thr Leu Ser Cys Lys Ile Ala Asp Phe Gly Leu  
370 375 380

Ala Arg Leu Ile Glu Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala Lys  
385 390 395 400

Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala Ile Asn Tyr Gly Thr Phe  
405 410 415

Thr Ile Lys Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Thr Glu Ile  
420 425 430

Val Thr His Gly Arg Ile Pro Tyr Pro Gly Met Thr Asn Pro Glu Val  
435 440 445

Ile Gln Asn Leu Glu Arg Gly Tyr Arg Met Val Arg Pro Asp Asn Cys  
450 455 460

Pro Glu Glu Leu Tyr Gln Leu Met Arg Leu Cys Trp Lys Glu Arg Pro  
465 470 475 480

Glu Asp Arg Pro Thr Phe Asp Tyr Leu Arg Ser Val Leu Glu Asp Phe  
485 490 495

Phe Thr Ala Thr Glu Gly Gln Tyr Gln Pro Gln Pro  
500 505

<210> 2

<211> 285

<212> PRT

<213> Recombinant baculovirus

&lt;400&gt; 2

Gln Thr Gln Lys Pro Gln Lys Pro Trp Trp Glu Asp Glu Trp Glu Val  
1 5 10 15

Pro Arg Glu Thr Leu Lys Leu Val Glu Arg Leu Gly Ala Gly Gln Phe  
20 25 30

Gly Glu Val Trp Met Gly Tyr Tyr Asn Gly His Thr Lys Val Ala Val  
35 40 45

Lys Ser Leu Lys Gln Gly Ser Met Ser Pro Asp Ala Phe Leu Ala Glu  
50 55 60

Ala Asn Leu Met Lys Gln Leu Gln His Gln Arg Leu Val Arg Leu Tyr  
65 70 75 80

Ala Val Val Thr Gln Glu Pro Ile Tyr Ile Ile Thr Glu Tyr Met Glu  
85 90 95

Asn Gly Ser Leu Val Asp Phe Leu Lys Thr Pro Ser Gly Ile Lys Leu  
100 105 110

Thr Ile Asn Lys Leu Leu Asp Met Ala Ala Gln Ile Ala Glu Gly Met  
115 120 125

Ala Phe Ile Glu Glu Arg Asn Tyr Ile His Arg Asp Leu Arg Ala Ala  
130 135 140

Asn Ile Leu Val Ser Asp Thr Leu Ser Cys Lys Ile Ala Asp Phe Gly  
145 150 155 160

Leu Ala Arg Leu Ile Glu Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala  
165 170 175

Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala Ile Asn Tyr Gly Thr  
180 185 190

Phe Thr Ile Lys Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Thr Glu  
195 200 205

Ile Val Thr His Gly Arg Ile Pro Tyr Pro Gly Met Thr Asn Pro Glu  
210 215 220

Val Ile Gln Asn Leu Glu Arg Gly Tyr Arg Met Val Arg Pro Asp Asn  
225 230 235 240

Cys Pro Glu Glu Leu Tyr Gln Leu Met Arg Leu Cys Trp Lys Glu Arg  
245 250 255

Pro Glu Asp Arg Pro Thr Phe Asp Tyr Leu Arg Ser Val Leu Glu Asp  
260 265 270

Phe Phe Thr Ala Thr Glu Gly Gln Tyr Gln Pro Gln Pro  
275 280 285

<210> 3.

$\langle 211 \rangle$     301

<212> PRT

<213> Artificial sequence

**<220>**

<223> See Figure 5 - ZAP70

<400> 3

Tyr Ser Asp Pro Glu Glu Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg  
1 5 10 15

Asp Asn Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly  
20 25 30

Ser Val Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Asp Val  
35 40 45

Ala Ile Lys Val Leu Lys Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu  
50 55 60

Met Met Arg Glu Ala Gln Ile Met His Gln Leu Asp Asn Pro Tyr Ile  
65 70 75 80

Val Arg Leu Ile Gly Val Cys Gln Ala Glu Ala Leu Met Leu Val Met  
85 90 95

Glu Met Ala Gly Gly Gly Pro Leu His Lys Phe Leu Val Gly Lys Arg  
100 105 110

Glu Glu Ile Pro Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ser  
115 120 125

Met Gly Met Lys Tyr Leu Glu Glu Lys Asn Phe Val His Arg Asp Leu  
130 135 140

Ala Ala Arg Asn Val Leu Leu Val Asn Arg His Tyr Ala Lys Ile Ser  
145 150 155 160

Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu Lys Val Lys  
35 40 45

Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser Pro Lys Ala  
50 55 60

Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser Val Asp Asn  
65 70 75 80

Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln  
85 90 95

Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp Tyr Val Arg  
100 105 110

Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn Trp Cys Val  
115 120 125

Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg Leu Val His  
130 135 140

Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro Gln His Val  
145 150 155 160

Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala Glu Glu Lys  
165 170 175

Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu  
180 185 190

Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp Val Trp Ser  
195 200 205

Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser Lys Pro Tyr  
210 215 220

Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu Lys Gly Glu  
225 230 235 240

Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met  
245 250 255

Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys Phe Arg Glu  
260 265 270

Leu Ile Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln Arg Tyr Leu  
275 280 285

Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp Ser  
290 295 300

Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val Val  
 305 310 315 320

Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser Ser Pro  
 325 330 335

Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser  
 340 345

<210> 5

<211> 298

<212> PRT

<213> Artificial sequence

<220>

<223> See Figure 5 - CDK2

<400> 5

Met Glu Asn Phe Gln Lys Val Glu Lys Ile Gly Glu Gly Thr Tyr Gly  
 1 5 10 15

Val Val Tyr Lys Ala Arg Asn Lys Leu Thr Gly Glu Val Val Ala Leu  
 20 25 30

Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu Gly Val Pro Ser Thr Ala  
 35 40 45

Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Asn His Pro Asn Ile Val  
 50 55 60

Lys Leu Leu Asp Val Ile His Thr Glu Asn Lys Leu Tyr Leu Val Phe  
 65 70 75 80

Glu Phe Leu His Gln Asp Leu Lys Lys Phe Met Asp Ala Ser Ala Leu  
 85 90 95

Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser Tyr Leu Phe Gln Leu Leu  
 100 105 110

Gln Gly Leu Ala Phe Cys His Ser His Arg Val Leu His Arg Asp Leu  
 115 120 125

Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu Gly Ala Ile Lys Leu Ala  
 130 135 140



Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Val Arg Thr Tyr Thr  
 145 150 155 160

His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly  
 165 170 175

Cys Lys Tyr Tyr Ser Thr Ala Val Asp Ile Trp Ser Leu Gly Cys Ile  
 180 185 190

Phe Ala Glu Met Val Thr Arg Arg Ala Leu Phe Pro Gly Asp Ser Glu  
 195 200 205

Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr Leu Gly Thr Pro Asp Glu  
 210 215 220

Val Val Trp Pro Gly Val Thr Ser Met Pro Asp Tyr Lys Pro Ser Phe  
 225 230 235 240

Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys Val Val Pro Pro Leu Asp  
 245 250 255

Glu Asp Gly Arg Ser Leu Leu Ser Gln Met Leu His Tyr Asp Pro Asn  
 260 265 270

Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala His Pro Phe Phe Gln Asp  
 275 280 285

Val Thr Lys Pro Val Pro His Leu Arg Leu  
 290 295

<210> 6

<211> 329

<212> PRT

<213> Artificial sequence

<220>

<223> See Figure 5 - PKA

<400> 6

Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu Ser Pro Ala Gln Asn Thr  
 1 5 10 15

Ala His Leu Asp Gln Phe Glu Arg Ile Lys Thr Leu Gly Thr Gly Ser  
 20 25 30

Phe Gly Arg Val Met Leu Val Lys His Lys Glu Thr Gly Asn His Tyr  
 35 40 45

Ala Met Lys Ile Leu Asp Lys Gln Lys Val Val Lys Leu Lys Gln Ile  
 50 55 60

Glu His Thr Leu Asn Glu Lys Arg Ile Leu Gln Ala Val Asn Phe Pro  
 65 70 75 80

Phe Leu Val Lys Leu Glu Phe Ser Phe Lys Asp Asn Ser Asn Leu Tyr  
 85 90 95

Met Val Met Glu Tyr Val Pro Gly Gly Glu Met Phe Ser His Leu Arg  
 100 105 110

Arg Ile Gly Arg Phe Ser Glu Pro His Ala Arg Phe Tyr Ala Ala Gln  
 115 120 125

Ile Val Leu Thr Phe Glu Tyr Leu His Ser Leu Asp Leu Ile Tyr Arg  
 130 135 140

Asp Leu Lys Pro Glu Asn Leu Leu Ile Asp Gln Gln Gly Tyr Ile Gln  
 145 150 155 160

Val Thr Asp Phe Gly Phe Ala Lys Arg Val Lys Gly Arg Thr Trp Thr  
 165 170 175

Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro Glu Ile Ile Leu Ser Lys  
 180 185 190

Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala Leu Gly Val Leu Ile Tyr  
 195 200 205

Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe Ala Asp Gln Pro Ile Gln  
 210 215 220

Ile Tyr Glu Lys Ile Val Ser Gly Lys Val Arg Phe Pro Ser His Phe  
 225 230 235 240

Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn Leu Leu Gln Val Asp Leu  
 245 250 255

Thr Lys Arg Phe Gly Asn Leu Lys Asn Gly Val Asn Asp Ile Lys Asn  
 260 265 270

His Lys Trp Phe Ala Thr Thr Asp Trp Ile Ala Ile Tyr Gln Arg Lys  
 275 280 285

Val Glu Ala Pro Phe Ile Pro Lys Phe Lys Gly Pro Gly Asp Thr Ser  
 290 295 300

Asn Phe Asp Asp Tyr Glu Glu Glu Ile Arg Val Ser Ile Asn Glu  
 305 310 315 320

Lys Cys Gly Lys Glu Phe Ser Glu Phe  
 325

<210> 7

<211> 275

<212> PRT

<213> Recombinant baculovirus

<400> 7

Met Asp Glu Trp Glu Val Pro Arg Glu Thr Leu Lys Leu Val Glu Arg  
 1 5 10 15

Leu Gly Ala Gly Gln Phe Gly Glu Val Trp Met Gly Tyr Tyr Asn Gly  
 20 25 30

His Thr Lys Val Ala Val Lys Ser Leu Lys Gln Gly Ser Met Ser Pro  
 35 40 45

Asp Ala Phe Leu Ala Glu Ala Asn Leu Met Lys Gln Leu Gln His Gln  
 50 55 60

Arg Leu Val Arg Leu Tyr Ala Val Val Thr Gln Glu Pro Ile Tyr Ile  
 65 70 75 80

Ile Thr Glu Tyr Met Glu Asn Gly Ser Leu Val Asp Phe Leu Lys Thr  
 85 90 95

Pro Ser Gly Ile Lys Leu Thr Ile Asn Lys Leu Leu Asp Met Ala Ala  
 100 105 110

Gln Ile Ala Glu Gly Met Ala Phe Ile Glu Glu Arg Asn Tyr Ile His  
 115 120 125

Arg Asp Leu Arg Ala Ala Asn Ile Leu Val Ser Asp Thr Leu Ser Cys  
 130 135 140

Lys Ile Ala Asp Phe Gly Leu Ala Arg Leu Ile Glu Asp Asn Glu Tyr  
 145 150 155 160

Thr Ala Arg Glu Gly Ala Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu  
                             165                            170                            175

Ala Ile Asn Tyr Gly Thr Phe Thr Ile Lys Ser Asp Val Trp Ser Phe  
                             180                            185                            190

Gly Ile Leu Leu Thr Glu Ile Val Thr His Gly Arg Ile Pro Tyr Pro  
                             195                            200                            205

Gly Met Thr Asn Pro Glu Val Ile Gln Asn Leu Glu Arg Gly Tyr Arg  
                             210                            215                            220

Met Val Arg Pro Asp Asn Cys Pro Glu Glu Leu Tyr Gln Leu Met Arg  
                             225                            230                            235                            240

Leu Cys Trp Lys Glu Arg Pro Glu Asp Arg Pro Thr Phe Asp Tyr Leu  
                             245                            250                            255

Arg Ser Val Leu Glu Asp Phe Phe Thr Ala Thr Glu Arg His His His  
                             260                            265                            270

His His His  
                             275

<210> 8

<211> 39

<212> DNA

<213> Artificial sequence

<220>

<223> DNA primer for baculovirus - See Example 8

<400> 8

cagaagagat ctatggagga cgagtgggag gttcccagg  
                             39

<210> 9

<211> 58

<212> DNA

<213> Artificial sequence

<220>

<223> DNA primer for baculovirus - See Example 8

<400> 9

ccacaggaat tcagtgatgg tggatgatgat gacgtgtggc cgtgaagaag tcctccag  
58

<210> 10

<211> 18

<212> DNA

<213> Artificial sequence

<220>

<223> DNA primer for baculovirus - See Example 8

<400> 10

gttctagtgg ttggctac  
18

<210> 11

<211> 23

<212> DNA

<213> Artificial sequence

<220>

<223> DNA primer of baculovirus - See Example 8

<400> 11

cctctacaaa tgtggtatgg ctg  
23